

PATENT

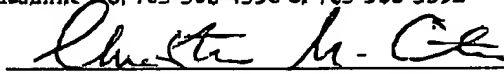
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Christine M. Citro

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Costas N. Karatzas et al.

Art Unit: 1632

Serial No.: 09/040,518

Examiner: Anne-Marie Baker

Filed: March 17, 1998

Customer No: 21559

Title: PRODUCTION OF BIOFILAMENTS IN TRANSGENIC ANIMALS

Assistant Commissioner for Patents
Washington, DC 20231

Declaration of Costas Karatzas Under 37 C.F.R. § 1.132

I declare:

1. I am a co-inventor of the subject matter described and claimed in the above-captioned patent application. I am educated and expert in the field of transgenic animal production, and I am familiar with the level of ordinary skill in the field at the time the above-captioned patent application was filed.

2. I have read the Office Actions issued in connection with this application; they are dated April 12, 2000, January 4, 2001 and July 18, 2001.

3. As I understand it, claim 2, directed to a non-human embryo encoding a spider biofilament, was rejected as not being useful. These embryos are useful because researchers working under my direction have used them to make adult animals that make biofilaments.

4. Researchers working at my direction have successfully carried out the following experiments to generate transgenic animals, which were described prophetically in the patent application. In March 1998, the time the application was filed, the description in the patent application of the methods used to generate the transgenic animals and to use them to produce biofilaments could have been successfully followed by a transgenic animal researcher of ordinary skill, without undue experimentation.

a) Using the methods described in the patent application, we generated three founder goats by pronuclear microinjection that were transgenic for the spider silk ADF-3 gene, under the control of the mouse WAP promoter and leader sequences as described in the patent application. One of these male goats (named "Zorro") was mated to produce 34 female goats of the next generation (F1), 10 of which were hormonally induced into lactation. One of these female goats produced more than 26 liters of milk. The ADF-3 biofilament protein was confirmed by tests that included Western blot analysis to be present in the milk.

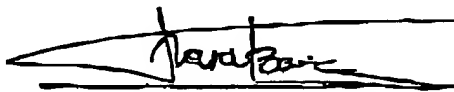
b) Using the methods described in the patent application, we generated nine founder goats (six female, three male) that were transgenic for the spider dragline silk MaSp I gene, under the control of the WAP promoter, which is described in the patent application. Six of these animals were generated using pro-nuclear microinjection, and three were generated using nuclear transfer. The six females were induced to lactation hormonally, and all six of them expressed the spider silk MaSpI protein, as confirmed by molecular weight measurement and recognition by MaSpI antibodies in a Western blot.

c) Using the methods described in the patent application, we generated eleven female founder goats which were transgenic for the spider silk MaSpII gene, under the control of the WAP promoter using nuclear transfer techniques. All of these animals produced the MaSpII protein at high levels (some made more than 1 gram of MaSpII protein per liter of milk), in over 27 liters of milk produced via hormonally induced lactation.

All statements made herein of my own knowledge are true, and all statements made on information and belief are believed to be true; further, these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

January 17, 2002

Date



Costas N. Karatzas, Ph.D.